

Pregnancy Induced Hypertension

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CONTRA COSTA REGIONAL
MEDICAL CENTER
NOON CONFERENCE SERIES

*DISCLOSURE OF CONFLICT OF
INTEREST*

- Speaker has nothing to disclose

PIH

- Gestational Hypertension (non-proteinuric)
- Preeclampsia
- Chronic Hypertension with Superimposed Preeclampsia
- Chronic Hypertension

Preeclampsia

- 5-8% US
- 3-14% worldwide
- US – 75% mild, 25% severe
- 10% of preeclampsia < 34 weeks
- Gestational HTN – 6%
- Chronic HTN – 3%

Gestational Hypertension

- Mild - systolic BP ≥ 140
diastolic BP ≥ 90
- Severe - systolic BP ≥ 160
diastolic BP ≥ 110
- 6 hours apart X 2
- Greater than 20 weeks

Preeclampsia

- Mild - systolic BP ≥ 140
diastolic BP ≥ 90
- Severe - systolic BP ≥ 160
diastolic BP ≥ 110
- 6 hours apart X 2
- Greater than 20 weeks
- 24 hour urine protein ≥ 0.3 grams
- $\sim 5\%$ present postpartum

Preeclampsia

- Systolic elevation of ≥ 30 mm Hg or diastolic elevation of ≥ 15 mm Hg are not used as diagnostic criteria for preeclampsia
- Edema no longer used for diagnosis

Criteria for severe preeclampsia

New onset proteinuric hypertension and at least one of the following:
Symptoms of central nervous system dysfunction:
Blurred vision, scotomata, altered mental status, severe headache (ie, incapacitating, "the worst headache I've ever had") or headache that persists and progresses despite analgesic therapy
Symptoms of liver capsule distention:
Right upper quadrant or epigastric pain
Nausea, vomiting
Hepatocellular injury:
Serum transaminase concentration at least twice normal
Severe blood pressure elevation:
Systolic blood pressure ≥ 160 mm Hg or diastolic ≥ 110 mm Hg on two occasions at least six hours apart
Thrombocytopenia:
Less than 100,000 platelets per cubic millimeter
Proteinuria:
5 or more grams in 24 hours
Oliguria <500 mL in 24 hours
Severe fetal growth restriction
Pulmonary edema or cyanosis
Cerebrovascular accident

Based on Diagnosis and Management of Preeclampsia and Eclampsia. American College of Obstetricians and Gynecologists. ACOG Practice Bulletin #33, January 2002 and Working Group Report on High Blood Pressure in Pregnancy. National Institutes of Health, Washington, DC 2000

Preeclampsia

Hemolysis

Elevated

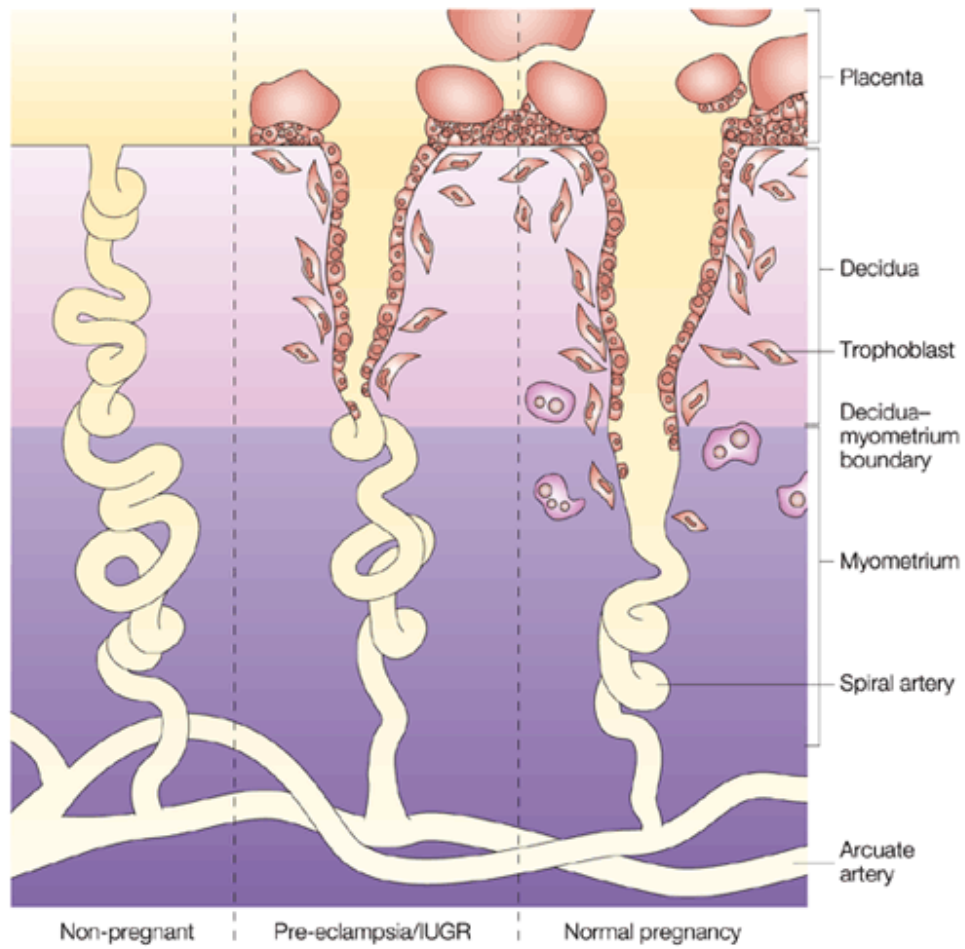
Liver functions

Low

Platelets

Preeclampsia

- Abnormal remodeling of spiral arteries
- Defective trophoblast differentiation
- Hypoperfusion
- Immunologic
- Genetic
- Endothelial dysfunction
- Inflammation
- ? Diet
- ?Increased sensitivity angiotensin II



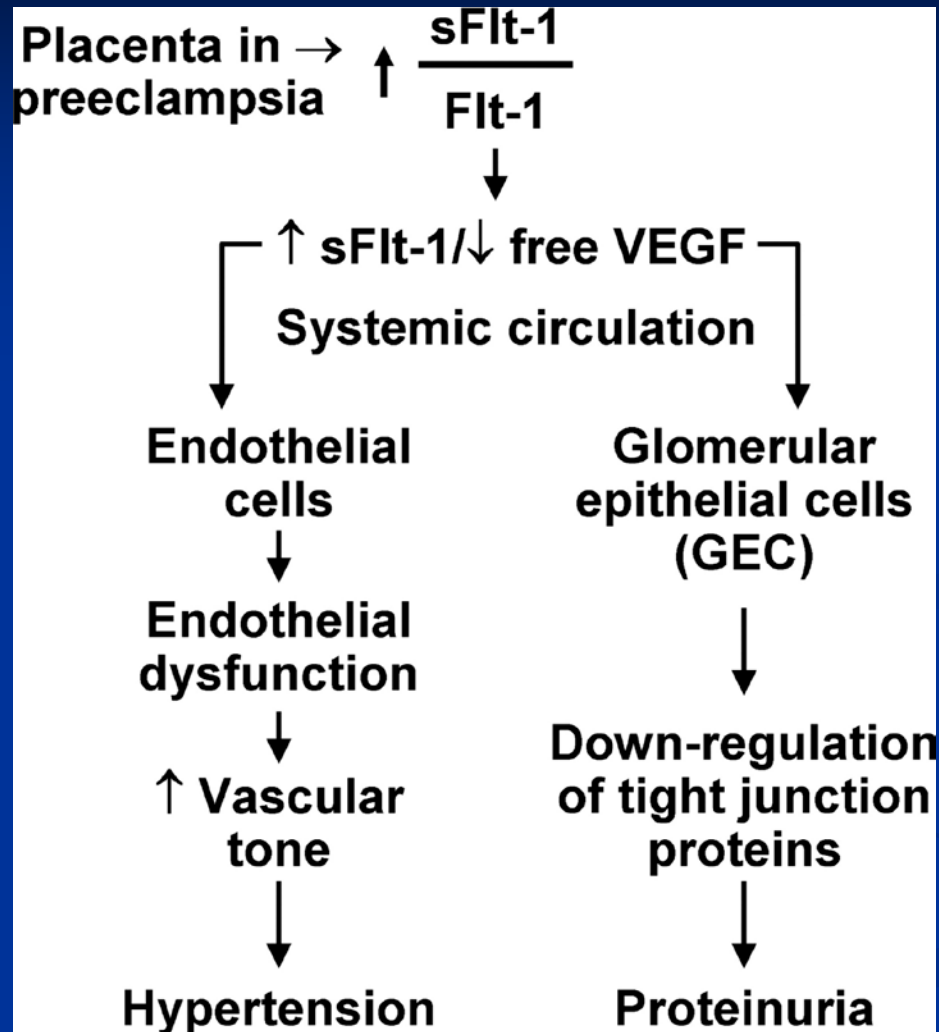
Preeclampsia

- Proangiogenic factors – VEGF, PlGF
- Antiangiogenic factors – sFlt-1, sEng
- Prostacyclin/thromboxane ratio
- What leads to release of sFlt-1?

Possible placental ischemia

Cause and effect

sFlt-1 hypothesis.



Garovic V D et al. Nephrol. Dial. Transplant. 2007;22:1136-1143

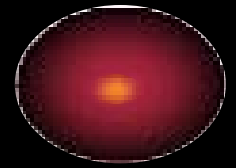
Preeclampsia

- Signs and symptoms related to microangiopathy of target organs
- Generalized endothelial dysfunction
- Disordered vascular tone
- Increased vascular permeability
- Abnormal endothelial expression of procoagulants
- Brain, liver, kidney, placenta

Preeclampsia Symptoms

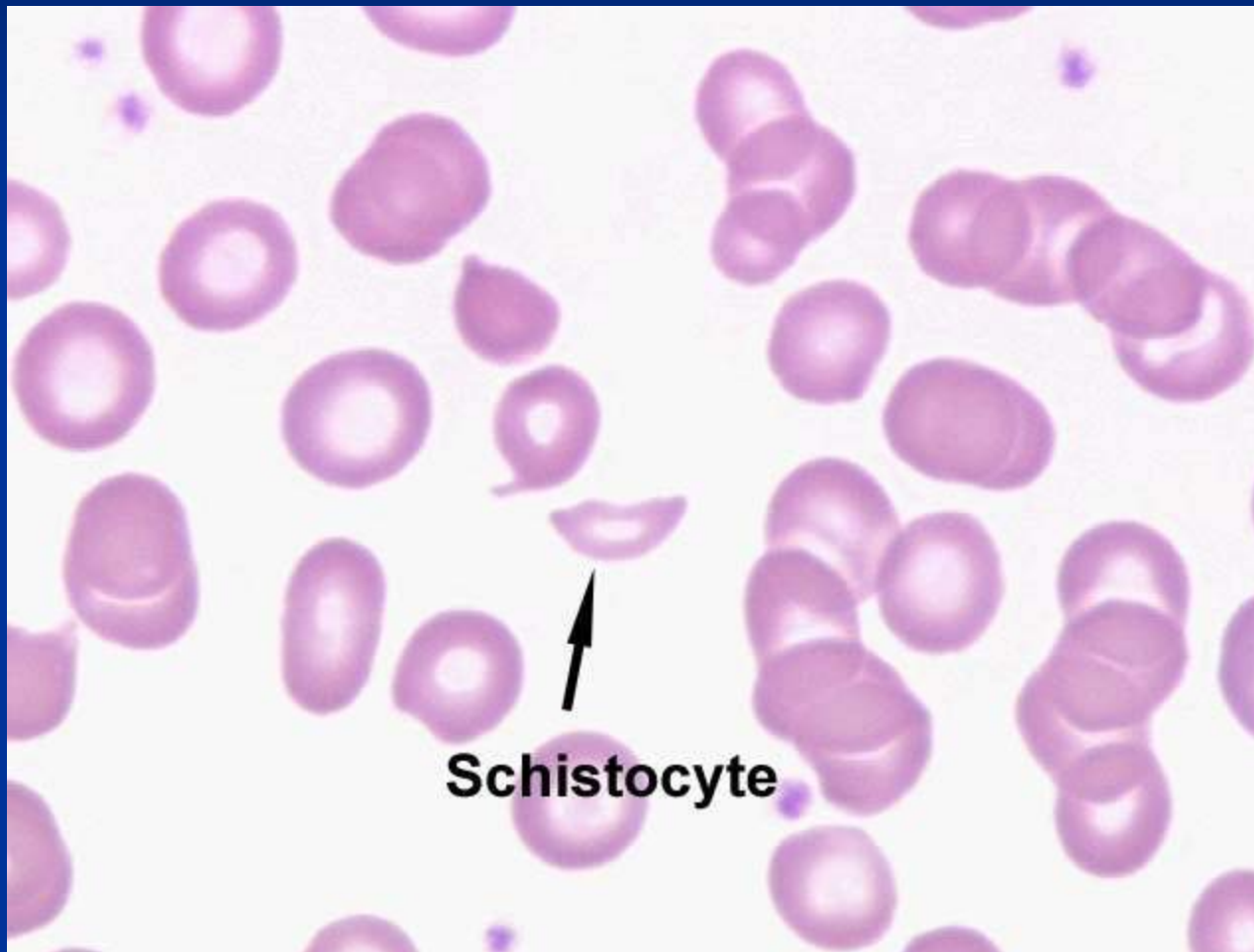


- Headache
- Visual changes - Scotomata, Blurring, Blindness
- Epigastric pain – RUQ, nausea, vomiting



Preeclampsia

- Hematocrit with smear
- Platelets
- Transaminases
- LDH
- Creatinine
- 24 hour urine protein
- Uric acid



Eclampsia

- New onset seizure in preeclamptic patient
- Usually preceded by severe headache
- 1/400 mild preeclampsics
- 2/100 severe preeclampsics
- Greek eklampsis, *a shining forth, sudden development*

Differential Diagnosis of Eclampsia

- Hypertensive encephalopathy
- Seizure disorder
- Hypoglycemia, hyponatremia
- Postpartum cerebral angiopathy (call-Fleming syndrome)
- Cerebral venous thrombosis
- Cerebral hemorrhage
- Postdural puncture syndrome
- Cerebral vasculitis

Gestational Hypertension

- 20-47% recurrence rate
- 15-25% progress to preeclampsia
- 40-50% if present at < 30 weeks
- Unknown pathophysiology - ? variant of preeclampsia

Gestational Hypertension

- Mild - similar outcomes to normotensive
- Severe – Increased risk of maternal/perinatal morbidity

IUGR, PTD, SGA, Abruption

Gestational Hypertension

- No antihypertensives for mild
- Labetalol for severe < 37 weeks
- Delivery at ~ 37 weeks
- Magnesium for severe

Management

- Treat BP ≥ 150 , ≥ 95 -100
- Acute – IV Labetalol, hydralazine, long acting oral Ca channel blocker
Sustained - Nitroprusside
- Bedrest +/-
- Prevention of stroke

HYPITAT

- Lancet. 2009 Sep 19;374(9694):979-88. Epub 2009 Aug 3.
- **Induction of labour versus expectant monitoring for gestational hypertension or mild pre-eclampsia after 36 weeks' gestation (HYPITAT): a multicentre, open-label randomised controlled trial.**
- [Koopmans CM](#), [Bijlenga D](#), [Groen H](#), [Vijgen SM](#), [Aarnoudse JG](#), [Bekedam DJ](#), [van den Berg PP](#), [de Boer K](#), [Burggraaff JM](#), [Bloemenkamp KW](#), [Drogtrop AP](#), [Frank A](#), [de Groot CJ](#), [Huisjes AJ](#), [Kwee A](#), [van Loon AJ](#), [Lub A](#), [Papatonis DN](#), [van der Post JA](#), [Roumen FJ](#), [Scheepers HC](#), [Willekes C](#), [Mol BW](#), [van Pampus MG](#); [HYPITAT study group](#).
- **Collaborators (20)** [van der Lans PJ](#), [Kleiverda G](#), [Heres MH](#), [van der Salm PC](#), [Rijnders RJ](#), [van Wijngaarden WJ](#), [van Huizen ME](#), [Stigter RH](#), [Akerboom BM](#), [Hasaart TH](#), [van Meir CA](#), [Pernet PJ](#), [Hanssen MJ](#), [Santema JG](#), [Copraai FJ](#), [van Beek E](#), [Sporken JM](#), [Aardenburg R](#), [Wijnen FJ](#), [Doornbos JP](#). Department of Obstetrics and Gynaecology, University Medical Centre, Groningen, Netherlands. c.m.koopmans@og.umcg.nl
- Comment in:
- **Abstract**
- **BACKGROUND:** Robust evidence to direct management of pregnant women with mild hypertensive disease at term is scarce. We investigated whether induction of labour in women with a singleton pregnancy complicated by gestational hypertension or mild pre-eclampsia reduces severe maternal morbidity.
- **METHODS:** We undertook a multicentre, parallel, open-label randomised controlled trial in six academic and 32 non-academic hospitals in the Netherlands between October, 2005, and March, 2008. We enrolled patients with a singleton pregnancy at 36-41 weeks' gestation, and who had gestational hypertension or mild pre-eclampsia. Participants were randomly allocated in a 1:1 ratio by block randomisation with a web-based application system to receive either induction of labour or expectant monitoring. Masking of intervention allocation was not possible. The primary outcome was a composite measure of poor maternal outcome--maternal mortality, maternal morbidity (eclampsia, HELLP syndrome, pulmonary oedema, thromboembolic disease, and placental abruption), progression to severe hypertension or proteinuria, and major post-partum haemorrhage (>1000 mL blood loss). Analysis was by intention to treat and treatment effect is presented as relative risk. This study is registered, number ISRCTN08132825.
- **FINDINGS:** 756 patients were allocated to receive induction of labour (n=377 patients) or expectant monitoring (n=379). 397 patients refused randomisation but authorised use of their medical records. Of women who were randomised, 117 (31%) allocated to induction of labour developed poor maternal outcome compared with 166 (44%) allocated to expectant monitoring (relative risk 0.71, 95% CI 0.59-0.86, p<0.0001). No cases of maternal or neonatal death or eclampsia were recorded.
- **INTERPRETATION:** Induction of labour is associated with improved maternal outcome and should be advised for women with mild hypertensive disease beyond 37 weeks' gestation.

Mild Preeclampsia

- Inpatient vs. outpatient
- Compliance issues
- Serial PIH labs 1-2 X / week
- Antenatal testing
- EFW U/S
- Steroids < 34 weeks
- Delivery \geq 37 weeks

Severe Preeclampsia

- ≥ 34 weeks – DELIVER
- Expectant management – intense inpatient monitoring
- Steroids
- Magnesium
- Contraindications to expectant management
- Refractory HTN (2400 mg labetalol/day, 120 mg Nifedipine/day) plt < 100K, doubling of transaminases, eclampsia, pulmonary edema, renal failure, severe headache, fetal distress, abruption, IUGR, oligohydramnios, labor

Severe Preeclampsia

- Expectant management of severe preeclampsia at less than 27 weeks' gestation: maternal and perinatal outcomes according to gestational age by weeks at onset of expectant management.

Bombrys AE, Barton JR, Nowacki EA, Habli M, Pinder L, How H, Sibai BM
Am J Obstet Gynecol. 2008;199(3):247.e1-6.

less than 23 and 0/7ths weeks (28 fetuses, 0 survivors)

23 and 0 to 6/7ths weeks (22 fetuses, 18 percent survival)

24 and 0 to 6/7ths weeks (26 fetuses, 58 percent survival)

25 and 0 to 6/7ths weeks (27 fetuses, 70 percent survival)

Magnesium Sulfate

- Prevention of Eclampsia (both severe and mild)
- 0.3-0.6% vs. 1.9-3.2% severe
- Decreased cerebral perfusion pressure (pure vasodilator increases cerebral perfusion pressure in preeclampsia i.e. Nimodipine)
- Prevents seizures – does not prevent progression of disease otherwise
- 4-6 gram load followed by 2 grams hour – modify based on creatinine level
- Contraindicated in patients with Myasthenia Gravis

Magnesium Sulfate

- 8-10 meq/L – loss of deep tendon reflexes
- 10-15 meq/L – respiratory paralysis
- 20-25 meq/L – cardiac arrest
- Reverse Magnesium toxicity with Calcium gluconate 1 gram IV over 5-10 minutes

Preeclampsia Sequelae

- Chronic HTN
- Cardiovascular disease
- End stage renal disease
- IUGR – increased risk cardiovascular disease later in life

Preeclampsia Risk Factors

- Prior preeclampsia (5-7% prior mild preeclampsia, 25-65% prior early severe preeclampsia)
- Pregestational DM
- Multiple gestation
- Obesity
- Chronic HTN
- APL syndrome
- AMA
- Nulliparity
- Family history

Preeclampsia Prevention

- Low dose ASA – Cochrane Database – modest but significant decrease in preeclampsia, preterm birth, perinatal death in patients at risk with pooled meta-analysis
- No good evidence for Ca, Vit C, Vit E, Fish oil

Preeclampsia Prediction

- ????????
- sFlt-1
- Uterine artery dopplers

Chronic Hypertension

- Treat severe
- Usually essential
- 10-25% superimposed preeclampsia
- IUGR, PTD, Abruptio

Chronic Hypertension

- Serial growth ultrasounds
- Antenatal testing
- Early delivery based on BP, fetal well being, progression to preeclampsia

Imitators of Severe Preeclampsia

- Acute fatty liver pregnancy (AFLP)
- Thrombotic thrombocytopenic
- purpura (TTP)
- Hemolytic uremic syndrome (HUS)
- Exacerbation of Lupus (SLE)
- Catastrophic APA syndrome
- Sepsis: viral
- Stroke

Imitators

(Laboratory Findings)

	HELLP	TTP/HUS	AFLP
■ Anemia		+++	-
■ Platelets	++	+++	
■ LDH	+++	++++	++
■ AST	++		++
■ Fibrinogen	N	N	Reduced
■ PT/PTT	N	N	Prolonged
■ Glucose	N	N	Reduced
■ Creatinine		++	++
■ Uric Acid	+	++	++
■ Ammonia	-	-	+
■ Bilirubin	+	++	+++

Imitators

(Clinical Findings)

■	HELLP	TTP/HUS	AFLP	Lupus
■ Hypertension	++	+		+
■ Proteinuria	++	++		+
■ Seizures	+	++	-	+
■ Purpura	++	++		-
■ Jaundice			++	-
■ Neurologic	+	++		
■ Renal failure		++	++	+
■ Fever	-	++	+	++

Cerebral CT/MRI findings in HELLP/Eclampsia & Imitators

	PRES	Infarcts	ICH	Angiopathy
■ HELLP/eclampsia	+++	+	++	
■ AFLP	+	-	+	-
■ TTP	++	+++	+	-
■ Lupus	-	++	-	++
■ CAPs	?	+++	-	-
■ CVT	+	+++	+	-